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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SULLIVAN, DANIEL M	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 07/20/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/974,882	NOLAN ET AL.	
	Examiner	Art Unit	
	Daniel M. Sullivan	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 July 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21 and 24-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21 and 24-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Non-Final Office Action is a reply to the Paper filed 7 July 2005 in response to the Final Office Action mailed 5 January 2005. Claims 21 and 24-34 were considered in the 5 January Office Action. No amendments were made in the 7 July Paper. Claims 21 and 24-34 are pending and under consideration.

Finality of the previous Office Action is hereby **withdrawn** in view of the new grounds for rejection set forth herein below.

Response to Arguments

Priority

The priority claim was previously denied because there is no support for the limitation "human or animal cell".

In response to the Examiner's arguments of record, Applicant points to the teaching at paragraph 0005, which teaches that FACS methods are known to be useful for sorting "human and animal" cells and at paragraph 0025, which teaches that various animal cell types are contemplated as host cells. Applicant also cites teachings that the methods described in the specification are useful in the context of gene therapy and directed to the concept of gene transfer as providing support for the claim limitation (7 July Paper, page 3).

These arguments have been fully considered and are deemed persuasive with regard to the genus "animal cell", which is reasonably supported by the recitation of "fibroblasts, parenchyma stem cells..." in paragraph 0025. However, the specification does not provide adequate descriptive support for the claimed method limited to practice

with "human" cells. As pointed out in the previous Office Action, the only mention of human cells is in the context of fluorophore labeling and FACS analysis of labeled cells. This is clearly not an explicit teaching of the claimed method practiced in human cells and does not provide implicit support for the limitation because the method claimed does not involve FACS analysis of labeled cells. All of the teachings with regard to gene transfer and the like cited by applicant are generic in nature and do not direct the skilled artisan to practicing the claimed method in humans. Applicant is further reminded that disclosure in an application that merely renders the later-claimed (by amendment) invention obvious is not sufficient to meet the written description requirement of 35 USC §112, first paragraph. *Lockwood, v. American Airlines, Inc.* 41 USPQ 2d 1961 at 1966 (CAFC, 1997).

For these reasons, the claimed method limited to practice with human cells constitutes subject matter that is not supported by the application as filed.

Specification

Objection to the specification under 35 U.S.C. 132 as containing new matter is withdrawn in view of the arguments and evidence provided in the 7 July Paper (page 2).

Applicant demonstrates that the originally filed application did include an incorporation by reference of the 09/453,610 application. Further, it is clear that the priority claim and incorporation by reference of provisional application 60/110,950 was an obvious error and it was Applicant's intention that the cited application be 60/110,951.

Claim Rejections - 35 USC § 112

Claims 21 and 24-34 **stand rejected** under 35 U.S.C. 112, first paragraph, as containing new matter.

Applicant's arguments have been fully considered but are not deemed persuasive in view of the record as a whole. For the reasons set forth herein above under the heading "Priority", the as filed application does not support the presently claimed method wherein a chromosome is introduced into a human cell. Therefore, the limitation constitutes impermissible new matter.

Claim Rejections - 35 USC § 102

Claims 21 and 24-34 **stand rejected** under 35 U.S.C. 102(b) as being anticipated by WO 00/34436 (hereinafter, '436).

As stated in the Office Action mailed 22 October 2003, the '436 publication teaches a method for introduction of at least one chromosome into a eukaryotic cell comprising contacting at least one chromosome substantially simultaneously with the application of an electric pulse to the cell, wherein the chromosome is encapsulated in a liposome or micelle (see especially claims 21 and 22). The '436 publication further teaches that the cells can be fibroblasts, parenchymal stem cells or hematopoietic stem cells, which are animal cells (see especially the paragraph bridging pages 8-9). Thus, the '436 publication teaches all of the limitations of claim 21. Further, the '436 publication teaches the method wherein transformation of the cell with at least one chromosome is verified by FACS according to the limitations of claims 24-26 (see especially the paragraph bridging pages 9-10). Still further, the '436 publication teaches the method

wherein the cell is contacted with an encapsulated single chromosome according to claims 27 and 31 (first full paragraph on page 8), and wherein the chromosome comprises 50% protein by weight according to claims 28-30 and 32-34 (third full paragraph on page 8). The '436 publication teaches a method comprising all of the limitations of the instant claims; therefore, the claims are anticipated by the art.

It is further noted that the '436 application contemplates introduction of yeast artificial chromosomes in the third full paragraph on page 8.

Although Applicant has sought to overcome the rejection by perfecting the priority claim and arguing that the limitations of the instant claims are supported by the original disclosure, the instant claims are not entitled to benefit of the previously filed applications because none of the applications contemplates the method comprising "introducing at least one chromosome into a human" (*Id.*).

New Grounds for Rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 21 and 24-34 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for introducing a chromosome into an animal cell, wherein the chromosome is a yeast artificial chromosome, does not reasonably provide enablement for the broad scope of the method wherein any gene-bearing DNA/protein complex, natural human chromosome, mammalian chromosome or

artificial chromosome. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Although the claims were not previously indicated to lack enablement for the method practiced *in vitro*, a careful review of the teachings of the instant application, priority documents and art of record reveals that the skilled artisan would not be able to make the and use the claimed invention commensurate with the scope of the protection sought.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to: (a) the nature of the invention; (b) the breadth of the claims; (c) the state of the prior art; (d) the amount of direction provided by the inventor; (e) the existence of working examples; (f) the relative skill of those in the art; (g) whether the quantity of experimentation needed to make or use the invention based on the content of the disclosure is "undue"; and (h) the level of predictability in the art (MPEP 2164.01 (a)).

Nature of the invention and Breadth of the claims: The claimed invention is drawn to a method for introducing an encapsulated chromosome into a eukaryotic cell by contacting the cell with a chromosome encapsulated in a liposome and an electric pulse under conditions sufficient to cause transformation of said cell by said chromosome, wherein the chromosome can be any gene-bearing DNA/protein complex, natural chromosome, mammalian chromosome or artificial chromosome.

State of the prior art and level of predictability in the art: Although the electroporation of yeast artificial chromosomes has been practiced in the art for a number of years predating Applicant's claimed invention, as has introduction of whole, native, protein-bearing chromosomes by microcell fusion, the art is silent with regard to introducing large chromosomal DNA's into cells by encapsulating said chromosomal DNA's in liposomes and contacting an animal cell with the encapsulated chromosome and an electrical pulse.

Amount of direction provided by the inventor and existence of working examples: The instant application does not contain a single working example of the claimed invention. In fact, the only guidance provide in the specification is simply a recitation of the process steps at, *e.g.*, paragraph 0038. In spite of the absence of any detailed description of "conditions sufficient to cause transformation of a cell by said chromosome" as recited in claim 21, Applicant's disclosure acknowledges that practicing the claimed method was unpredictable at the time of filing. For example, the disclosure of the 60/110,951 application, incorporated by reference, teaches in the paragraph bridging pages 1-2:

> Currently, only two methods have practical feasibility for the rapid delivery of very large (greater than 100 kb) pieces of intact DNA. These two methods are (1) electroporation and (2) liposome mediated delivery. However, whether either of these processes can deliver intact DNA of the size and constituency of a chromosome is not clearly known. A human chromosome is of the order of 1-10 megabase (1-10 million bases, or 10,000 kb) and is also ~50% by weight protein. The large size of this molecular complex demands special consideration of the methodology used to introduce it into a living cell. Specifically, an obvious concern is how to deliver such an object without physically damaging either it, or the cell. While electroporation or lipid assisted delivery may have some success in doing this, the efficiency and quality of such a transfer are difficult to control.

Likewise, in paragraph 0024, the instant application teaches, "[t]echnical barriers in the art had previously rendered difficult the insertion of chromosomes comprising greater than about 100 kb in length."

Relative skill of those in the art and quantity of experimentation needed to make or use the invention: Although the relative level of skill in the art is high, the skilled artisan would not be able to practice the claimed invention without undue experimentation to establish conditions sufficient to provide a useful degree of transformation of an animal cell according to the instant method.

The physiological art is recognized as unpredictable (MPEP 2164.03). As set forth in *In re Fischer*, 166 USPQ 18 (CCPA 1970), compliance with 35 USC §112, first paragraph requires that:

> the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art. In cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws. In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved

The unpredictability of the art is clearly acknowledged in the instant application and priority documents, yet the disclosure fails to provide detailed instructions, guidance and working examples so as to enable one of skill in the art to practice the invention commensurate with the scope of the subject matter claimed.

Given the unpredictable and undeveloped state of the art as acknowledged by applicant, and the paucity of guidance and working examples, it would require undue experimentation to enable the invention commensurate with the claimed methods recited.

The instant invention, as claimed, falls under the "germ of an idea" concept defined by the CAFC. The Court stated, "patent protection is granted in return for an enabling disclosure, not for vague intimations of general ideas that may or may not be workable". The Court continues, stating, "the specification, not knowledge in the art, must supply the novel aspects of an invention in order to constitute adequate enablement". (see *Genentech Inc. v. Novo Nordisk A/S* 42 USPQ2d 1001, at 1005). The methods of the claimed invention constitute such a "germ of an idea" and are therefore not enabled.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel M Sullivan whose telephone number is 571-272-0779. The examiner can normally be reached on Monday through Friday 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Daniel M. Sullivan, Ph.D.
Examiner
Art Unit 1636

DANIEL M. SULLIVAN
PATENT EXAMINER